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## Using In Vitro HTS Methods to Identify Endocrine Disruptors

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## **Abstract**

Current testing for endocrine-active substances utilizes a battery of *in vitro* and *in vivo* screening assays. The Tox21 program includes multiple *in vitro* assays conducted in a high-throughput screening (HTS) format that are relevant to the estrogen receptor (ER) pathway and could be used to identify substances with potential ER activity *in vivo*. NICEATM compared results from 16 HTS ER pathway assays with published results from uterotrophic studies. We reviewed the literature for 1777 substances tested in ToxCast/Tox21 and identified 191 substances with uterotrophic data. Each study was scored based on adherence to a set of minimum criteria established by NICEATM for guideline-like protocols. To facilitate direct comparison for select ER-active substances, models were built using experimental data and structure-based predictions for metabolic clearance and plasma protein binding to estimate the oral equivalent doses that would result in steady-state blood concentrations equivalent to the HTS *in vitro* point of departure values. This strategy may be sufficient to screen for ER activity independent of *in vivo* tests. This project was funded in whole or in part with Federal funds from the NIEHS, NIH under Contract No.HHSN27320140003C.

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